Brain structure, number magnitude processing, and math proficiency in 6- to 7-year-old children born prematurely: a voxel-based morphometry study

Starke, Marc ; Kiechl-Kohlendorfer, Ursula ; Kucian, Karin ; Pupp Peglow, Ulrike ; Kremser, Christian ; Schocke, Michael ; Kaufmann, Liane

Abstract: The aim of the present voxel-based morphometry study was to examine the link between brain structure and number skills in a group of 6-7-year-old children born prematurely, which are considered to be an at-risk population for mathematical learning disabilities. Therefore, gray and white matter density values were extracted from brain areas previously reported to be relevant for number processing in developing brain systems and, thereafter, correlated with response time results tapping semantic number knowledge [i.e. numerical distance effect (NDE) derived from a number comparison task] as well as with general math proficiency (as indexed by a standardized calculation test). Behavioral results disclosed a significant NDE, thus indicating well-established number magnitude representations for one-digit numerals in our study group. Significant positive correlations between gray matter and NDE emerged in parietal regions (including the right anterior inferior and the left superior parietal lobe) and in the right superior temporal gyrus. Moreover, white matter and NDE were negatively correlated in the right anterior inferior parietal lobe and the right inferior frontal gyrus. Overall, our results are novel insofar as they show that in 6-7-year-old children born prematurely, individual differences in gray and white matter structures are associated with numerical skills. Importantly, in our study group the observed link between brain structure and behavioral performance emerges only regarding an experimental task tapping semantic number knowledge, whereas general math proficiency does not seem to be related to individual differences in brain structure in our study group.

DOI: https://doi.org/10.1097/WNR.0b013e32836140ed

Brain structure, number magnitude processing and math proficiency in 6- to 7-year-old children born prematurely: A voxel-based morphometry study

by

Marc **Starke**[1], Ursula **Kiechl-Kohlendorfer**[1], Karin **Kucian**[2,3], Ulrike **Pupp Peglow**[1], Christian **Kremser**[4], Michael **Schocke**[4], Liane **Kaufmann**[1,5]

[1]Innsbruck Medical University, Department of Pediatrics II, Innsbruck, Austria

[2]Center for MR-Research, University Children´s Hospital Zurich, Switzerland

[3]Children´s Research Center, University Children´s Hospital Zurich, Switzerland

[4]Innsbruck Medical University, Department of Radiology, Innsbruck, Austria

[5]General Hospital, Department of Psychiatry and Psychotherapy A, Hall in Tyrol, Austria

Corresponding address:

Liane Kaufmann, PhD

General Hospital

Department of Psychiatry and Psychotherapy A

Milser Strasse 10

A-6060 Hall in Tyrol

E-mail: liane.kaufmann@tilak.at

Conflict of interest: none declared

Funding sources: The work of M Starke and L Kaufmann was supported by the Anniversary Fund of the Austrian National Bank (grant number 13.454).

Abstract

The aim of the present voxel-based morphometry study was to examine the link between brain structure and number skills in a group of 6- to 7-year-old children born prematurely, which are considered to be an at-risk population for mathematical learning disabilities. Therefore, gray and white matter density values were extracted from brain areas previously reported to be relevant for number processing in developing brain systems and thereafter, correlated with response time results tapping semantic number knowledge (i.e., numerical distance effect/NDE derived from a number comparison task) as well as with general math proficiency (as indexed by a standardized calculation test). Behavioral results disclosed a significant NDE, thus indicating well established number magnitude representations for one-digit numerals in our study group. Significant positive correlations between gray matter and NDE emerged in parietal regions (including the right anterior inferior and the left superior parietal lobe) and in the right superior temporal gyrus. Moreover, white matter and NDE were negatively correlated in the right anterior inferior parietal lobe and the right inferior frontal gyrus. Overall, our results are novel insofar as they disclose that in 6- to 7-year-old children born prematurely individual differences in gray and white matter structures are associated with numerical skills. Importantly, in our study group the observed link between brain structure and behavioral performance emerges only regarding an experimental task tapping semantic number knowledge, while general math proficiency does not seem to be related to individual differences in brain structure in our study group.

Word count: 245

Key words

Prematurity, numerical cognition, number magnitude representation, math proficiency, voxel-based morphometry, gray and white matter, anterior inferior parietal cortex, superior temporal gyrus, inferior frontal gyrus.

Introduction

Compared with term-born children those born prematurely are reported to have a much higher risk to develop reading and calculation difficulties [1,2]. Moreover, structural and functional brain abnormalities seem to be frequently associated with prematurity [3]. Nonetheless, studies investigating brain correlates of numerical processing in children born prematurely are sparse. The present study aims to fill this gap by examining children born prematurely that are just about to learn mathematics and that are known to have a high risk to develop math difficulties later on. Below, we will briefly summarize our current understanding of the neural correlates of number processing in developing brain systems.

With respect to *functional brain imaging*, accumulating evidence suggests that fronto-parietal regions play a key role for number processing in adults [4] and children alike [5,6]. Notably, number-relevant brain regions (mostly located in inferior and superior parietal as well as (pre)frontal cortex) seem to be modulated by age [5,6], number format and math proficiency [6]. In both children and adults, the intraparietal sulcus (IPS) has been identified as a core region for semantic number processing, while the left angular gyrus (AG) mediates number fact retrieval and possibly, the automatic mapping of arithmetic symbols and problems onto memory representations [4-7]. Yet another parietal region, namely the posterior superior parietal lobe modulates spatial attention on the so-called mental number line [8]. Moreover, extraparietal activations associated with number processing are consistently reported –among others- in (pre)frontal brain regions and are thought to reflect the involvement of supporting mechanisms such as working memory, updating and monitoring [4-7,8].

As regards *structural imaging*, to the present only few studies investigated brain morphology in children with average and subaverage math skills. Results of a voxel-based morphometry (VBM) study revealed that compared with math-proficient peers, 15-year-olds with math difficulties displayed reduced gray matter (GM) in the left (intra)parietal lobe [9]. Likewise, structural abnormalities including the inferior and superior (intra)parietal lobes were reported to be associated with math proficiency in term-born school children with and without developmental dyscalculia (DD) [10,11]. Moreover, DD seems to be associated with extra-parietal structural deficiencies in frontal regions (anterior cingulate cortex, inferior frontal gyrus, dorsolateral prefrontal cortex [10]) as well as in the ventral visual stream (fusiform gyrus, anterior temporal cortex [11], parahippocampal gyrus [10,11]). Similarly, children with DD displayed reduced white matter (WM) in number-relevant temporo-parietal regions [10,11], most probably reflecting deficiencies related to memory representations underlying the storage of semantic number knowledge. Finally, recent DTI findings suggest that individual differences in 7- to 9-year-old's math skills are related to WM integrity in the left inferior longitudinal fasciculus (being part of the ventral visual stream) [12] which has been interpreted as evidencing children's ease to process Arabic numerals. Overall, there is converging evidence from both functional and structural developmental imaging studies, that inferior and superior (intra)parietal lobes seem to be key regions for (semantic) number processing, while extra-parietal regions including (pre)frontal and temporal regions seem to modulate task-dependent and supporting functions such as working memory and semantic memory representations [5,6,8].

Study aim and working hypotheses

Our approach was hypothesis-driven: we capitalized on brain regions previously reported to be crucially involved in children's number processing [6] (Table 1). First, GM and WM volumes were extracted from number-relevant brain regions upon employing VBM. Second, the respective density values were correlated with two performance measures: a reaction time (RT) measure indexing semantic number knowledge and a general estimate of math proficiency. Our *working hypotheses* were twofold: (i) We expected robust RT effects (i.e., so-called numerical distance effect/NDE), (ii) we argued that GM and WM may correlate with the NDE (indexing semantic number knowledge) and with math proficiency (i.e., performance on a standardized calculation test).

While general math proficiency requires the integrity of many aspects of domain-specific (i.e., arithmetical) and domain-general (e.g., attention, visual-spatial) knowledge and thus, depends on the integrity of distributed neural networks, semantic number knowledge is modulated by (intra)parietal brain regions [5,6,8]. Hence, semantic number knowledge might be more likely to be associated with morphological alterations in predefined number-relevant (intra)parietal brain regions in our group of 6- and 7-year-olds.

Materials and methods

Participants were 16 right-handed children born prematurely with a gestational age of <32 weeks or a birthweight ≤1500 g (mean age 7.2 years, range 6.3 to 7.9 years). Excluded were children with severe neurological or neuropsychiatric diseases and neuropathological findings in the neonatal period. All participating children had average *intellectual abilities* at time of testing (German-language version of the Wechsler Intelligence Scale for Children-4th revision [13]).

Math proficiency was assessed upon utilizing the *standardized calculation test* TEDI-MATH [14]. TEDI-MATH total scores comprise various subscales tapping basic numerical and calculation skills (e.g., counting procedures and principles, approximate number knowledge, base-10-knowledge, speeded calculations, incomplete calculations, conceptual knowledge, text problems). Math performance varied considerably, percentile ranks (PR) ranging from 15 to 96. Though none of the children qualified for a diagnosis of DD (PR <10), several children may be regarded at risk to develop calculation difficulties (PR 10<25).

Semantic number knowledge was examined by employing a PC-administered number comparison task, requiring children to indicate by button-press the larger of two horizontally presented equally sized single-digit Arabic numerals (small distance trials: 2-3, 3-4, 4-5, 6-7, 7-8; large distance trials: 2-6, 3-7, 4-8). The NDE (calculated upon comparing small- and large distance trials) indexes semantic number knowledge and has been found to decrease with increasing age and expertise [15]. Upon acknowledging the substantial RT variability frequently observed in children's data, relative RT differences were calculated as follows: For each participant, the mean RT difference between small and large distance trials was divided by the individual's overall mean RT upon solving the very same task, thus yielding a relative NDE (relNDE) which was used in the further analyses.

The study was approved by the ethical committee of Innsbruck Medical University. Written informed consent was obtained from parents of participating children.

Structural brain imaging and preprocessing

High-resolution T1-weighted structural images were acquired using a 1.5 Tesla magnet (Siemens Magnetom Avanto; acquisition matrix 256 x 256; repetition time 1800ms; echo time 2.92ms; inversion time 1100ms; flip angle 15°; field of view 256mm; 160 slices; slice thickness 1.0mm; voxel size 1.0mm x 1.0mm x 1.0mm; parallel imaging Grappa 2 mode). Image processing was performed using the Statistical Parametric Mapping package SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). VBM was conducted with the VBM8 plugin for SPM8 (developed by Chrisitan Gaser, University of Jena). T1-weighted images were segmented into GM, WM and cerebrospinal fluid probability maps and transformed into Montreal Neurological Institute (MNI) space using a fitted pediatric average template [16]. Gender and age were entered as reference data. Images were smoothed using an 8 mm full width at half maximum Gaussian kernel. Number-relevant regions of interest (ROIs) were defined as 12mm spheres on coordinates obtained from a recent meta-analysis on developmental fMRI studies [6] (Table 1). Mean density values were extracted from the segmented probability maps for each ROI and every participant. The resulting 512 values (16 ROIs x 16 children x 2 types of brain matter) represent the estimated GM and WM volumes within the predefined ROIs that were used for further correlation analyses. ROI definitions and GM/WM extraction were carried out upon utilizing the SPM8 plugin marsbar.

Statistical analyses

Associations between brain morphology (GM, WM) and behavioral performance (relNDE, math proficiency) were examined by performing correlation analyses, using age and intelligence as covariables. For the sake of simplicity, we will use the abbreviation NDE whenever we refer to relNDE below.

Results

The NDE was highly significant regarding both RT ($t(15)=6.16$, $P<.001$) and accuracy ($t(15)=4.87$, $P<.001$), thus indicating that children were significantly slower and less accurate upon classifying adjacent number pairs (mean RT 1467msec, standard deviation (SD) 269msec; mean AC 84.6%, SD 8.6%) compared with large distance trials (mean RT 1321msec, SD 269msec; mean AC 93.8%, SD 7.1%). Because accuracies were high, only RT (i.e., NDE) was used for further analyses. The relation between math proficiency and NDE was negative, but non-significant ($r=-.13$, $P=.653$).

As regards the association between NDE and brain morphology, significant correlations emerged with GM and WM in several previously reported ROIs [6]. In the right anterior inferior parietal cortex, the NDE correlated significantly with both GM ($r=.68$, $P=.008$) and WM ($r=-.56$, $P=.036$) (Table 1, Figure 1). Further significant correlations between *GM* and NDE emerged in the left superior parietal cortex ($r=.62$, $P=.019$) and the right superior temporal gyrus ($r=.59$, $P=.026$). Moreover, in the left anterior inferior parietal cortex the association between NDE and GM approached significance ($r=.53$, $P=.053$). Finally, *WM* was found to correlate significantly with NDE in the right inferior frontal gyrus ($r=-.57$, $P=.035$). No other previously reported ROI [6] yielded significant correlations between NDE and GM or WM (Table 1).

Likewise, correlations between brain morphology and math proficiency were not significant (neither regarding GM nor WM).

< Table 1 and Figure 1>

Discussion

The present study was hypotheses-driven and targeted at examining whether in 6- to 7-year-old children born prematurely individual differences in numerical skills are related to brain morphology in number-relevant ROIs [6].

Behavioral findings revealed robust NDE regarding both accuracy and latency, which is consistent with our working hypothesis. Thus, our findings suggest that even young children born prematurely that are just about to learn formal mathematics have rather well-established semantic number representations for one-digit Arabic numerals. Moreover, math proficiency as indexed by a standardized calculation test [14] varied considerably across the group (PR ranging from 15 to 96), which is according to expectation as prematurity is associated with a high risk to develop (mathematical) learning disabilities [1,2,9]. Finally, a negative but non-significant correlation emerged between NDE and math proficiency, thus suggesting that the NDE decreases with increasing expertise [15].

Correlations between brain morphology and NDE were significant (even after controlling for age and intelligence), while those with a measure of general math proficiency were not. Importantly, individual differences regarding the NDE (indexing semantic number knowledge) were associated with brain structure in some, but not all of the predefined ROIs found to be key for children's symbolic number processing [6].

Significant correlations between NDE and GM were positive and restricted to regions in the right anterior inferior parietal cortex including the anterior IPS, the left superior parietal cortex as well as the superior temporal gyrus. Furthermore, the link between NDE and GM in the left anterior inferior parietal cortex approached significance (r=.53, P=.053). The latter results are compatible with previous imaging findings reporting a tight link between inferior and superior (intra)parietal cortices and numerical thinking [9,18,19]. Similarly, the relation between superior temporal brain structures and number processing has been reported previously in children and may reflect memory-based processing of Arabic numerals [8-10].

Correlations with WM were negative and located in the right anterior inferior parietal cortex including the IPS and right inferior frontal gyrus. Thus, the right anterior IPS was the only region in which the NDE correlated significantly with both GM and WM. The latter findings nicely fit previous developmental functional imaging findings reporting a tight link between the NDE and the right anterior inferior parietal lobe (bordering the IPS) [19]. Furthermore, our findings disclosing that individual differences in numerical skills are related to WM in fronto-parietal brain structures are consistent with previous DTI findings showing that higher WM integrity of the anterior superior longitudinal fasciculus, a fiber bundle connecting parietal and frontal cortex, is related to higher math proficiency [20,21].

Please note that the observed negative correlations between WM and NDE imply larger WM volumes being associated with smaller NDE. Consistent with previous findings in typically developing same-age children [15], NDE was negatively (but non-significantly) related with math proficiency, thus suggesting that children with higher math proficiency displayed smaller NDE. Hence, larger WM volumes in fronto-parietal ROIs go along with better math skills (i.e., smaller NDE) in our study group, which is compatible with previous DTI findings in adolescents and young adults [20,21] and further corroborate the existing developmental literature disclosing a positive relation between WM increases and cognitive skill level [22].

Our results suggesting that children with a larger NDE (and poorer math skills) have larger GM and smaller WM volumes in number-relevant brain regions are somewhat difficult to reconcile with previous structural imaging findings reporting that poor math skills in children are related to *reduced* GM and *reduced* WM in number-relevant regions [9-11]. Potential explanations for the inconsistent findings are as follows: First, while previous studies were conceptualized as between-group comparisons including children with and without DD [10-11], we conducted a within-group comparison including slightly younger children with varying skill levels not qualifying a DD diagnosis. Second, correlational findings reported here should be interpreted as evidencing a (positive or negative) relation that need not necessarily imply a deficiency (in one or the other direction). Third, increased GM as well as decreased WM seems to be associated with prematurity and has been interpreted as reflecting disorganized cortical development [22,23].[1] Though in general, cognitive deficiencies seem to be accompanied by reductions in both WM and GM [9-12,22], atypical developmental trajectories may be associated with relative GM increases [22-24]. Interestingly, longitudinal findings disclosed that compared with term-born children those born prematurely display significantly less WM increases (in frontal, temporal and parietal cortex) and less GM reductions (in temporal and parietal cortex) [23].

Finally, our failure to find a significant correlation between brain structure and math proficiency as indexed by a standardized calculation test is in contrast to recent DTI findings in typically developing 17- to 18-year-olds [21]. However, the two studies are not readily comparable to each other because math aptitude tests measure different functions in the two age groups and furthermore, cerebral development (and its relation to skill acquisition) may be differentially affected by premature and mature birth [3,22,23].

To the best of our knowledge, this is the first study targeted at elucidating the link between brain morphology and numerical skills in young children born prematurely. Notably, correlations reported above survived corrections for age and intelligence and

[1] While typical cerebral development is characterized by linear increases of WM volume, GM volume follows a nonlinear developmental trajectory that is characterized by an inverted U-shaped curve [24]. Thus, GM reductions are developmentally appropriate and thought to be driven by synaptic pruning processes.

may be considered relevant as all correlation coefficients were ≥.5, thus indicating moderate effect sizes [25]. Our results are novel as they reveal that individual differences in brain morphology are related to semantic number knowledge (but not to general math proficiency) in 6- and 7-year-old prematurely born children known to be at risk to develop math difficulties later on. Furthermore, our findings suggest that already in young children who are just about to learn formal mathematics semantic number knowledge and brain morphology are tightly intertwined in number-relevant regions in frontal, parietal and temporal areas.

Acknowledgements

We are grateful to all participating children and their parents for their time and efforts devoted to this study. M. Starke and L. Kaufmann were supported by the Anniversary fund of the Austrian National Bank (grant number 13.454).

References

1. Aylward GP. Neurodevelopmental outcomes of infants born prematurely. J Dev Behav Pediatr. 2005;26:427-440
2. Saigal S, den Ouden L, Wolke D, Hoult L, Paneth N, Streiner DL, et al. School-age outcomes in children who were extremely low birth weight from four international population-based cohorts. Pediatrics. 2003;112:943-950
3. Peterson BS. Brain imaging studies of the anatomical and functional consequences of preterm birth for human brain development. Annals N Y Acad Sci. 2003;1008:219-237
4. Arsalidou M, Taylor MJ. Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. Neuroimage. 2011;54(3):2382–2393
5. Houde O, Rossi S, Lubin A, Joliot M. Mapping numerical processing, reading, and executive functions in the developing brain: an fMRI meta-analysis of 52 studies including 842 children. Dev Sci. 2010;13(6):876–885
6. Kaufmann L, Wood G, Rubinsten O, Henik A. Meta-analyses of developmental FMRI studies investigating typical and atypical trajectories of number processing and calculation. Dev Neuropsychol. 2011;36:763-787
7. Cantlon JF, Brannon EM, Carter EJ, Pelphrey KA. Functional imaging of numerical processing in adults and 4-y-old children. PLoS Biology. 2006;4(5):e125
8. Kucian K, Kaufmann L, von Aster M. Brain correlates of numerical disabilities. In: Cohen Kadosh R, Dowker A, editors. Oxford handbook of numerical cognition. NY: Oxford University Press; in press.
9. Isaacs EB, Edmonds CJ, Lucas A, Gadian DG. Calculation difficulties in children of very low birthweight: a neural correlate. Brain. 2001;124(Pt 9):1701-1707
10. Rotzer S, Kucian K, Martin E, von Aster M, Klaver P, Loenneker T. Optimized voxel-based morphometry in children with developmental dyscalculia. Neuroimage. 2008;39:417-422

11. Rykhlevskaia E, Uddin LQ, Kondos L, Menon V. Neuroanatomical correlates of developmental dyscalculia: combined evidence from morphometry and tractography. Front Hum Neurosci. 2009;3:51

12. van Eimeren L, Niogi SN, McCandliss BD, Holloway ID, Ansari D. White matter microstructures underlying mathematical abilities in children. Neuroreport. 2008;19(11):1117–1121

13. Petermann F, Petermann U. (Hrsg.). Hamburg-Wechsler-Intelligenztest für Kinder IV (HAWIK-IV). Bern: Verlag Hans Huber; 2008.

14. Kaufmann L, Nuerk H-C, Graf M, Krinzinger H, Delazer M, Willmes K. TEDI-MATH: Test zur Erfassung numerisch-rechnerischer Fertigkeiten für 4-8 Jährige. Bern: Verlag Hans Huber; 2009.

15. DeSmedt B, Verschaffel L, Ghesquière P. The predictive value of numerical magnitude comparison for individual differences in mathematics achievement. J Exp Child Psychol. 2009;103:469-479

16. Wilke M, Holland SK, Altaye M, Gaser C. Template-O-Matic: A toolbox for creating customized pediatric templates. Neuroimage. 2008;41:903-913

17. Mai JK, Paxinos G, Voss T. Atlas of the Human Brain, 3rd Edition. San Diego: Elsevier Academic Press; 2007.

18. Cantlon JF, Davis SW, Libertus ME, Kahane J, Brannon EM, Pelphrey KA. Inter-parietal white matter development predicts numerical performance in young children. Learn Individ Differ. 2011;21(6):672-680

19. Holloway ID, Ansari D. Developmental specialization in the right intraparietal sulcus for the abstract representation of numerical magnitude. J Cogn Neurosci. 2010;22(11):2627-2637

20. Tsang JM, Dougherty RF, Deutsch GK, Wandell BA, Ben-Shachar M. Frontoparietal white matter diffusion properties predict mental arithmetic skills in children. Proc Natl Acad SCi U S A. 2009;106(52):22546–22551

21. Matejko AA, Price GR, Mazzocco MM, Ansari D. Individual differences in left parietal white matter predict math scores on the Preliminary Scholastic Aptitude Test. Neuroimage. 2013;66:604-610

22. Hüppi P. Growth and development of the brain and impact on cognitive outcome. Nestle Nutr Workshop Ser Pediatr Program. 2010;65:137-149 (discussion 149-151)

23. Ment LR, Kesler SR, Vohr B, Katz KH, Baumgartner H, Schneider KC et al. Longitudinal brain volume changes in preterm and term control subjects during late childhood and adolescence. Pediatr. 2009;123(2):503-511

24. Giedd JN, Rapaport JL. Structural MRI of pediatric brain development: What have we learned and where are we going? Neuron. 2010;67(5):728-734

25. Ferguson CJ. An effect size primer: A guide for clinicians and researchers. Prof Psychol: Res Pract. 2009;40(5):532-538

Table 1. Results of the correlation analyses targeted at examining association strengths between GM and WM volumes extracted from brain areas reported to be relevant for children's symbolic number processing (meta-analysis I [6]) and semantic number knowledge (i.e., relative NDE derived from a number comparison task).

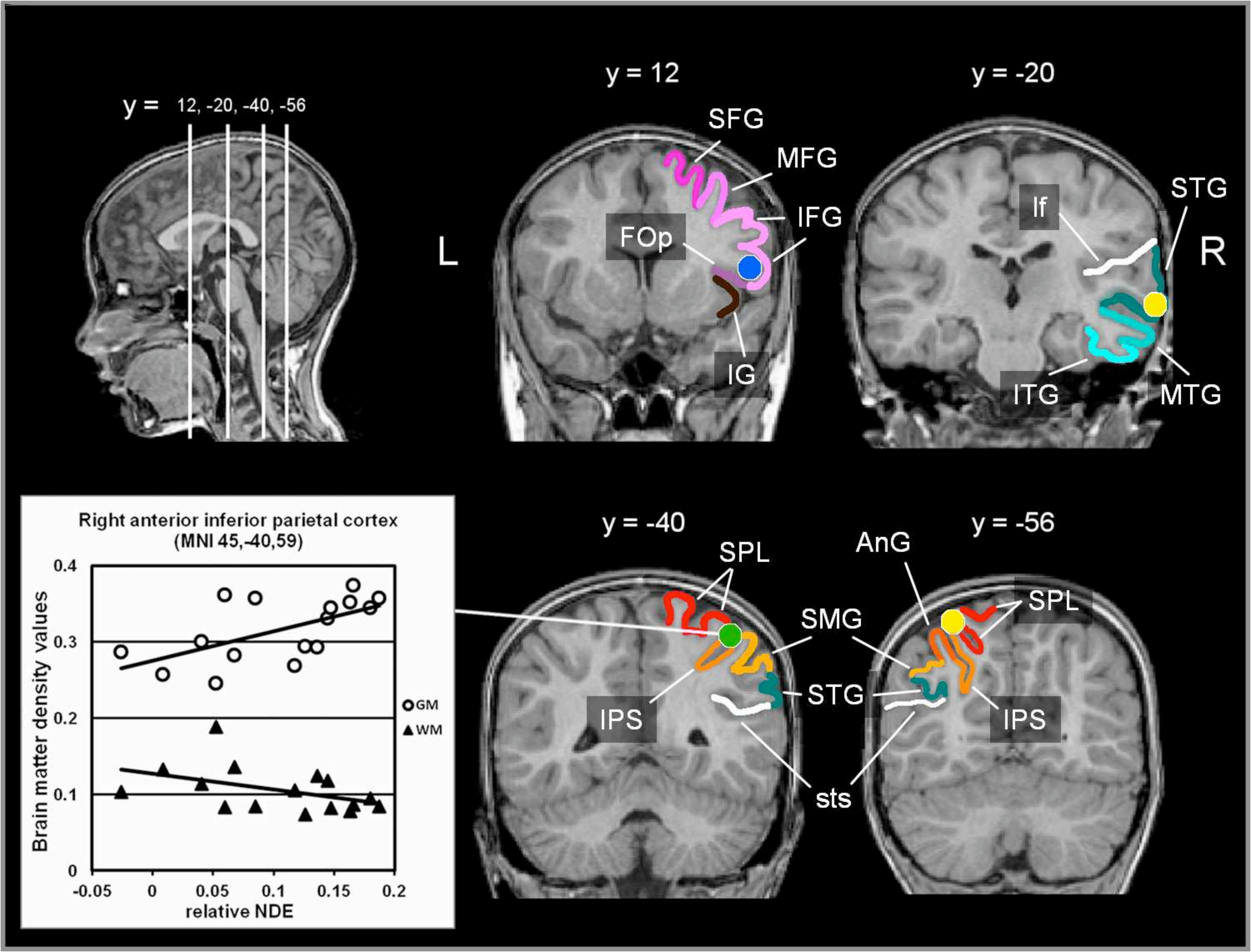
Anatomical region	Side	MNI Coordinates			GM *r* (*P*)	WM *r* (*P*)
		x	y	z	NDE	NDE
Medial frontal gyrus	R	10	28	44	*.23 (.437)*	*-.37 (.198)*
Inferior frontal gyrus	R	53	12	9	*.22 (.449)*	*-.57 (.035)**
Anterior cingulate gyrus	R	6	17	21	*.06 (.846)*	*-.31 (.282)*
Cingulate gyrus	L	-20	-41	27	*-.34 (.240)*	*.09 (.772)*
Insula	R	40	14	-7	*.33 (.249)*	*-.14 (.635)*
Precentral gyrus	R	45	12	32	*-.10 (.736)*	*-.32 (.265)*
Premotor cortex	L	-7	13	55	*.26 (.366)*	*-.37 (.192)*
Premotor cortex	L	-64	8	18	*.23 (.428)*	*-.42 (.137)*
Premotor cortex	R	10	13	50	*.06 (.841)*	*.11 (.699)*
Superior temporal gyrus	R	72	-20	-4	*.59 (.026)**	*-.20 (.501)*
Anterior inferior parietal cortex	L	-55	-24	23	*.53 (.053)°*	*-.08 (.796)*
Anterior inferior parietal cortex	R	45	-40	59	*.68 (.008)***	*-.56 (.036)**
Superior parietal cortex	L	-28	-56	66	*.62 (.019)**	*-.28 (.341)*
Cerebellar tuber	L	-38	-65	-24	*.49 (.078)*	*-.27 (.344)*
Cerebellar declive	R	27	-60	-17	*.48 (.085)*	*.46 (.100)*
Cerebellar declive	M	1	-72	-11	*.24 (.402)*	*-.15 (.618)*

Notes: **highly significant at $P<.01$; *significant at $P<.05$; °approaching significance

Figure caption

Figure 1: Schematic representation of correlations between GM/WM volumes and NDE in brain regions previously reported to support symbolic number processing in children [6]. Color blobs denote regions with significant correlations (yellow=GM, blue=WM, green=GM and WM). Colored lines represent relevant neighboring gyri and sulci (red/orange=parietal structures, greenish/turquoise=temporal structures, pink/rose=frontal structures). *Abbreviations* (adopted from [17][2])*:* AnG=angular gyrus, FOp=frontal operculum, IFG=inferior frontal gyrus, IG=insular gyrus, ITG=inferior temporal gyrus, IPS=intraparietal sulcus, lf=lateral fissure, MFG=middle frontal gyrus, MTG=middle temporal gyrus, SFG=superior frontal gyrus (lateral part), SMG=supramarginal gyrus, SPL=superior parietal lobule, STG=superior temporal gyrus, sts=superior temporal sulcus.

[2] See also Petrides M. The Human Cerebral Cortex. An MRI Atlas of the Sulci and Gyri in MNI Stereotaxic Space. London: Academic Press; 2011



y = 12, -20, -40, -56
y = 12
y = -20
SFG
MFG
IFG
FOp
IG
L
R
If
STG
ITG
MTG
Right anterior inferior parietal cortex
(MNI 45,-40,59)
Brain matter density values
relative NDE
0.4
0.3
0.2
0.1
0
-0.05
0
0.05
0.1
0.15
0.2
GM
WM
y = -40
y = -56
SPL
AnG
SMG
STG
IPS
sts